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INTERNATIONAL NONPROPRIETARY NAMES (INN) FOR BIOLOGICAL AND BIOTECHNOLOGICAL SUBSTANCES

(A REVIEW)

Programme on International Nonproprietary Names (INN)

Quality Assurance and Safety: Medicines (QSM)

Medicines Policy and Standards (PSM) Department

INTRODUCTION

More than 50 years ago, WHO established the International Nonproprietary Name (INN) Expert Group/ WHO Expert Committee on Specifications for Pharmaceutical Preparations, to assign nonproprietary names to medicinal substances, so that each substance would be recognized globally by a unique name. These INNs do not give proprietary rights, unlike a trade mark, and can be used freely as they are public property.

INNs have been assigned to biological products since the early days of the INN Programme. As well as many names for individual substances, animal insulin preparations were given an INN in Recommended list 3 in 1959. In the period up to 1980, names were assigned to antibiotics, synthetic peptides, hormones and other proteins. Compounds related by structure and/or function are given stems to aid recognition by health professionals. The *–actid*e synthetic corticotrophin analogues is an example.

In 1982, the name *insulin human* was proposed for the recombinant protein identical to natural human insulin and since then names have been assigned to a growing number of recombinant products. Within the INN Programme, names have not been assigned to natural human blood products or vaccines. The Expert Committee for Biological Standardisation (ECBS) has adopted the scientific names of the biological products within the definitions of respective requirements.

Since the time that *insulin human* became the first recommended INN (rINN) for a recombinant product, the range of biological/biotechnology products has increased in size and complexity. For example, new stems have been introduced for tissue plasminogen activators (*-plase*) among other groups. Analogues of a given recombinant protein produced in different cell systems have been classified using Greek indicators in the sequence of introduction: erythropoietin (*epoetin alfa*, *beta* and so on) and glycoprotein hormones (*follitropin*) are examples. In the 1990s, a systematic scheme for naming monoclonal antibodies was implemented, based on the stem *–mab*, which indicates the origin (mouse, human, etc) of the antibody and its intended use: tumour, immunomodulator and so on.

With the scientific and technical developments currently taking place, new products of biotechnology and other biological products are being introduced and more products can be expected for treatment or prevention of disease. Examples of such new products include recombinant blood products, transgenic products (human proteins expressed in animals or plants), products for gene therapy and novel vaccines.

As this area is becoming more and more complex and challenging, the INN Expert Group on Biological and Biotechnology Products has requested the WHO-INN Secretariat to prepare a working document intended to summarize and review the past and present INN situation in this field.

This document therefore presents an inventory of the policy decisions taken by the INN Expert Group during all these years of change, and of the names assigned to biological and biotechnological substances. Considering the potential for further developments in the field of biologicals, this review is intended to be a *living document* which will be regularly updated to include new policies, and future INNs assigned.
Comments and suggestions from all interested parties are most welcome and will be presented to the INN Expert Group for their consideration and for possible incorporation in future updates of this review.

4.19 Interferons

Interferon was published as an INN in 1962 with a general definition based on the origin and activity, e.g. "a protein formed by the interaction of animal cells with viruses capable of conferring on animal cells resistance to virus infection".

The name was revised in the 1980s when human interferon and its variations *alfa*, *beta* and *gamma* were produced by recombinant biotechnology. The INN Expert Group would have preferred to replace the old INN interferon by alfaferon, betaferon and gammaferon; however, this approach was barred as these names had already been registered as trade-marks. The system adopted was then to take interferon alfa, interferon beta and interferon gamma, and to provide, when necessary, for further distinction by additional numbers, or in the case of mixtures, by additional codes.

interferon alfa (73), interferon alfacon-1 (77), interferon beta (73), interferon gamma (73), peginterferon alfa-2a (84), peginterferon alfa-2b (84).

4.20 Monoclonal antibodies

The common stem for monoclonal antibodies is *-mab*.

INNs for monoclonal antibodies alphabetically by origin:

***-axomab* (pre-substem, rat-murine hybrid)**

catumaxomab (93), ertumaxomab (93)

***-omab* (mouse origin)**

afelimomab (80), altumomab (80), anatumomab mafenatox (86), arcitumomab (74), bectumomab (81), besilesomab (92), biciromab (66), capromab (80), detumomab (80), dorlimomab aritox (66), edobacomab (80), edrecolomab (74), elsilimomab (89), enlimomab (80), enlimomab pegol (77), epitumomab (82), epitumomab cituxetan (89), faralimomab (81), gavilimomab (84), ibritumomab tiuxetan (86), igovomab (86), imciromab (66), inolimomab (80), lemalesomab (86), maslimomab (66), minretumomab (80), mitumomab (82), nacolomab tafenatox (80), nerelimomab (81), odulimomab (81), oregovomab (86), satumomab (81), sulesomab (86), taplitumomab paptox (84),

technetium (^{99m}Tc) fanolesomab (86), technetium (^{99m}Tc) nofetumomab merpentan (81), technetium (^{99m}Tc) pintumomab (86), telimomab aritox (66), tositumomab (80), vepalimomab (80), zolimomab aritox (80).

***-umab* (human origin)**

adalimumab (85), adecatumumab (90), atorolimumab (80), belimumab (89), bertilimumab (88), denosumab (94), exbivirumab (91), golimumab (91), ipilimumab (94), iratumumab (94), lerdelimumab (86), libivirumab (91), mapatumumab (93), metelimumab (88), morolimumab (79), nebacumab #(66), ofatumumab (93), panitumumab (91), pritumumab (89), raxibacumab (92), regavirumab (80), sevirumab (66), stamulumab (94), ticilimumab (94), tuvirumab (66), votumumab (80), zalutumumab (93), zanolimumab (92), ziralimumab (84).

***-ximab* (chimeric origin)**

abciximab (80), basiliximab (81), cetuximab (82), clenoliximab (77), ecromeximab (87), galiximab (89), infliximab (77), keliximab (81), lumiliximab (90), pagibaximab (93), priliximab (80), rituximab (77), teneliximab (87), vapaliximab (87), volociximab (93).

***-zumab* (humanized origin)**

alemtuzumab (83), apolizumab (87), aselizumab (88), bapineuzumab (93), bevacizumab (86), bivatuzumab (86), cantuzumab mertansine (89), cedelizumab (81), certolizumab pegol (90), daclizumab (78), eculizumab (87), efalizumab (85), epratuzumab (82), erlizumab (84), felvizumab (77), fontolizumab (87), gemtuzumab (83), inotuzumab ozogamicin (92), labetuzumab (85), lintuzumab (86), matuzumab (88), mepolizumab (81), natalizumab (79), nimotuzumab (94), ocrelizumab (94), omalizumab (84), palivizumab (79), pascolizumab (87), pertuzumab (89), pexelizumab (86), ranibizumab (90), reslizumab (85), rovelizumab (81), ruplizumab (83), sibrotuzumab (86), siplizumab (87), sontuzumab (94), tadocizumab (94), talizumab (89), tefibazumab (92), tocilizumab (90), toralizumab (87), trastuzumab (78), tucotuzumab celmoleukin (94), urtoxazumab (90), visilizumab (84), yttrium ^{90}Y tacatuzumab tetraxetan (93).

4.21 Oxytocin derivatives

The common stem for oxytocin derivatives is *-tocin*.

argiprestocin (13), aspartocin (11), carbetocin (45), cargutocin (35), demoxytocin (22), nacartocin (51), oxytocin (13).